UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/677,752	10/03/2000	W. James Jackson	7969-087	5261

20583 7590 05/14/2002

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 05/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/677,752	Applicant(s) JACKSON, W. JAMES	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,15-24,31,32,41,57-59 and 73-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,15-24,31,32,41,57-59 and 73-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's response in paper No. 10 to the first Office Action in paper No. 6. The amendment and Exhibit A (consisting of a PMPE amino acid sequence and nucleotide sequence encoding PMPE) and Exhibit B (consisting of a declaration under 37 C.F.R. 1.131 with attached exhibits 1-12-C, a statement regarding the microorganism deposit, submission of formal drawings and a revised information disclosure statement) submitted December 3, 2001 are acknowledged. Claims 5, 8-14, 25-30, 33-40, 50-56 and 60-72 have been cancelled. Claims 1-4, 6-7, 15, 31, 41 and 57-59 have been amended. Claims 73-78 have been added.

2. The Declaration and attached exhibits 1-12-C filed on December 2, 2001 under 37 CFR 1.131 are sufficient to overcome the Probst et al (WO 00/34483, published June 15, 2000) reference.

3. In view of Applicant's amendment the following Objections and Rejections have been withdrawn:

a) Objection to the Declaration, page 2, paragraph 2 of previous Office action.
b) Objection to the Drawings, page 2, paragraph 3 of previous Office action.
c) Objection to the Information Disclosure Statement, pages 2-3, paragraphs 4 and 5 of previous Office action.
d) Objection to the specification, page 3, paragraph 6, of previous Office action.
e) Rejection of claims 15-24, 31-34 and 41 under U.S.C. 112, first paragraph, pages 5-6, paragraph 8 of the previous Office action.
f) Rejection of claims 1-7, 15-24, 31-32, 41 and 57-59 under 35 U.S.C. 112, second paragraph, page 6, paragraph 9 of previous Office action.

g) Rejection of claim 4 under 35 U.S.C. 112, second paragraph, page 6, paragraph 10 of previous Office action.
h) Rejection of claims 15-24, 31-32 and 41 under U.S.C. 102(a), page 8, paragraph, 12 of the previous Office action.
i) Rejection of claims 57-59 under 35 U.S.C. 102(a), page 9, paragraph 13 of the previous Office action.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

5. The rejection of claims 1-4, 6-7, 15-24, 31-32, 41 and 57-59 under 35 U.S.C. 112, first paragraph is maintained for reasons set forth in paper 6, pages 3-5, paragraph 7 of the previous Office Action.

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses SEQ ID NO: 2 or 4 which corresponds to the amino acid sequence that encodes a PMPE or PMPI polypeptide. Claims 1-7 are directed to sequences that are substantially homologous to SEQ ID NO: 2 or 4, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)
With the exception of SEQ ID NO:2 or 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d

1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 2 or 4 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant urges that the specification is sufficiently described to meet the statutory written description requirement. Applicant further urges that Exhibit A presents a BLAST comparison which shows SEQ ID No:2 and two sequences encoding PMPE that are 90% identical and therefore provides the full scope of the present claims.

Applicant's arguments filed December 3, 2001 in paper No. 10 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing on the record to show that the specification is enabled for the full scope of the claims and therefore does not meet the written description requirement as set forth in 35 U.S.C. 112, first paragraph. Applicant has not shown enablement for variants of SEQ ID NO. 2. The specification discloses only one species within the scope of the genus: SEQ ID NO:2. Exhibit A submitted by the Applicant used BLAST to discover two other species within the scope of the genus. There is no description of the mutational sites that exist in nature. The specification discloses only SEQ ID NO:2 which corresponds to an isolated polypeptide of *Chlamydia* spp. While use of BLAST and other sequence comparison tools are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable

expectation of success in obtaining similar activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure. The nature of the species within a genus are variant structures. In the present state of the art, the structure of one does not provide guidance to the structure of others and is insufficient to support the claimed invention.

6. The rejection of claims 1-4 and 6 under U.S.C. 102(b) as being anticipated by Stephens et al is maintained for the reasons set forth in paper 8, pages 7-8, paragraph 11 of the previous Office action.

The rejection was on the grounds that Stephens et al teach a protein that is 98% identical to the SEQ ID NO: 2 of the claimed invention. The amino acid sequence fragments of SEQ ID NO: 5-34 are included in the amino acid sequences of SEQ ID NO: 2 or 4. Therefore, the amino acid fragments that are associated with SEQ ID NO: 2 are included in the teachings of Stephens et al. Stephens et al teach a total of nine genes named pmp encoding relating proteins. The gene family was located in two clusters with one gene being separate (p. 757, 2nd column, last paragraph and Figure 1A, p. 756). For each of the predicted proteins, the COOH-terminal residue was phenylalanine and some of the family contained predicted cleavable signal peptide leader sequences (PmpC, PmpD, PmpE, and PmpI). These attributes suggest that the proteins are outer membrane proteins. Each was a different size and quite dissimilar in sequence (9 to 42 % amino acid identity), but all were found to be related and shared tetrapeptide repeat motifs organize d in the NH_2-terminal half of the protein (p. 757, 3rd column, 1st paragraph and Figure 1B, p. 756).

The Applicant urges that Stephens et al discloses the theoretical existence and function of gene encoding a protein which is 98% identical to SEQ ID No:2 and that the proteins of Stephens et al are not obtained in the isolated form. Applicant urges that Stephens et al does not teach or suggest the use of PMPE and does not provide any evidence that PMPE can be used as a vaccine to ameliorate disease caused by

infection with *Chlamydia*. Applicant further urges that Stephens et al does not teach fragments of PMPE and do not teach a composition comprising a polypeptide fused to an amino acid sequence comprising a (H)6) affinity domain and do not teach a vaccine composition comprising PMPE and an adjuvant or immunostimulatory compound.

Applicant's arguments filed December 3, 2001 in paper No. 10 have been fully considered but are not persuasive. The applicant's arguments are not commensurate in scope with the claimed invention. The applicant is arguing limitations that are not in the claimed invention. The claimed invention is drawn to an isolated putative membrane polypeptide of a *Chlamydia spp.* and not a vaccine. It is the Examiner's position that there is nothing on the record to show that the claimed PMPE polypeptide is not the same as the PMPE polypeptide of the prior art. The polypeptide of Stephens et al is a "probable outer membrane protein E", accession No. E71460 from serotype D, strain UW3/Cx of *Chlamydia trachomatis* (see NCBI database printout). The polypeptide of Stephens et al begins with a methionine amino acid residue denoting an open reading frame. The Applicant has provided no side-by-side comparison to show that the PMPE polypeptide of the prior art is not the same as the claimed polypeptide.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as anticipated by Longbottom et al *(FEMS Microbiology Letters 164, 1998, p. 111-117).*

Claims 1-2 and 4 are drawn to a polypeptide comprising an isolated putative membrane protein polypeptide of a *Chlamydia spp.* having a molecular weight between 90 and 115 kDa as determined by SDS polyacrylamide gel electrophoresis which protein specifically binds an antibody that specifically binds to a protein comprising the amino acid sequence of SEQ ID No:2.

Longbottom et al teach a putative outer membrane protein from *Chlamydia psittaci* (see the Abstract). Longbottom et al teach that the putative outer membrane protein is 90 kDa as determined by SDS electrophoresis (see Figure 3, page 115). Longbottom et al teach that surface localization on the elementary bodies (EB) indicates the importance of these proteins as protective antigen candidates. Longbottom et al suggest that protein components exposed on the EB outer membrane surface are crucial to the successful infection of host cells and are therefore appropriate targets for vaccine development (pages 111-112). Longbottom et al further suggest that putative outer membrane proteins play a role in protective immunity since they are present in chlamydial outer membrane complexes (page 112, 1st column). The amino acid sequence would be inherent in the teachings of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 1 and 6 are rejected under 35 U.S.C. 102(e) as anticipated by Probst et al *(U.S. Patent No. 6,166,177, published December 26, 2000).*

Claims 1 and 6 are drawn to a peptide fragment of the PMPE polypeptide of claim 1 which fragment is at least 8 amino acids in length and specifically binds an antibody that specifically binds to the protein comprising the amino acid sequence of SEQ ID No.2.

Probst et al teach antibodies both polyclonal and monoclonal that bind to the polypeptides of their invention (column 1, lines 63-65). Probst et al teach *Chlamydia* antigens that recognize a T cell line that recognizes both *Chlamydia trachomatis* and *Chlamydia pneumonia* (column 5, lines 56-64). Probst et al teach polypeptides comprising at least an immunogenic portion of one or more Chlamydial antigens use alone or in combination to detect Chlamydial infection in a patient (column 1, lines 56-59). Probst et al also teach that immunogenic portions comprise at least 5 amino acid residues but preferably about 10 to 20 amino acid residues (column 1, lines 39-49).

Since the Office does not have the facilities for examining and comparing applicant's peptide fragment with the peptide fragment of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the peptide fragment of the prior art does not possess the same material structural and functional characteristics of the claimed peptide fragment). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 1, 15-24, 41 and 75-76 are rejected under 35 U.S.C. 102(e) as anticipated by Probst et al *(U.S. Patent No. 6,166,177, published December 26, 2000).*

Claims 1, 15-24, 41 and 75-76 are drawn to the PMPE polypeptide of claim 1 and a pharmaceutically acceptable carrier.

Probst et al teach pharmaceutical compositions and vaccines comprising polypeptides that contain at least one antigenic portion of a Chlamydial antigen (see the Abstract). Probst et al teach that any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions. Probst teach that these carriers include water, saline, alcohol, a fat or wax or a buffer (column 9, lines 14-28). Probst et al teach that a variety of adjuvants may be employed in the vaccines of this invention to enhance the immune response. Probst et al teach that the adjuvants may include aluminum hydroxide, mineral oil, Freund's Incomplete Adjuvant, Freund's Complete Adjuvant, Merck Adjuvant 65, alum, biodegradable microspheres, monophosphoryl lipid A and quil A (column 9, lines 29-41).

Since the Office does not have the facilities for examining and comparing applicant's vaccine with the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Please note: The Examiner is viewing claim 57 as a product by process claim. The Examiner is viewing claim 57 to read on a genus of isolated recombinant PMPE polypeptides that are produced by a method comprising culturing a host cell containing a nucleic acid molecule comprising SEQ ID NO:1. The scope of claim 57 encompasses PMP polypeptides from *Chlamydia trachomatis*, *Chlamydia pneumonia*, *Chlamydia psittaci* and *Chlamydia pecorum* (specification pages 11 and 24). The Examiner is also viewing the "recombinant PMPE polypeptides" to have the same characteristics as the native PMPE polypeptides.

10. Claims 57-59 and 73-74 are rejected under 35 U.S.C. 102(e) as anticipated by Longbottom et al *(FEMS Microbiology Letters 164, 1998, p. 111-117).*

Claims 57-59 and 73-74 are drawn to an isolated recombinant PMPE polypeptide produced by a method comprising culturing a host cell containing a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No:1 fused to a nucleotide sequence encoding a histidine affinity ($(H6)_6$) domain under conditions suitable for expression of said PMPE polypeptide and recovering said recombinant PMPE polypeptide.

Longbottom et al teach a putative outer membrane protein from *Chlamydia psittaci* (see the Abstract). Longbottom et al teach that the putative outer membrane protein is 90 kDa as determined by SDS electrophoresis (see Figure 3, page 115). Longbottom et al teach that surface localization on the elementary bodies (EB) indicates the importance of these proteins as protective antigen candidates. Longbottom et al suggest that protein components exposed on the EB outer membrane surface are crucial to the successful infection of host cells and are therefore appropriate targets for vaccine development (pages 111-112). Longbottom et al further suggest that putative

outer membrane proteins play a role in protective immunity since they are present in chlamydial outer membrane complexes (page 112, 1st column).

Although the reference appears to disclose the same purified polypeptides claimed by the applicant's, the reference does not disclose that the purified polypeptides produced by the same claimed process. However, the purification or production of protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marsosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Since the Office does not have the facilities for examining and comparing applicant's polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 57-59 and 73-74 are rejected under 35 U.S.C. 102(e) as anticipated by Stephens et al, *(Science, Volume 282, October 23, 1998).*

Claims 57-59 and 73-74 are drawn to an isolated recombinant PMPE polypeptide produced by a method comprising culturing a host cell containing a nucleic acid

molecule comprising the nucleic acid sequence of SEQ ID No:1 fused to a nucleotide sequence encoding a histidine affinity ($(H6)_6$) domain under conditions suitable for expression of said PMPE polypeptide and recovering said recombinant PMPE polypeptide.

Stephens et al teach a protein that is 98% identical to the SEQ ID NO: 2 of the claimed invention. The amino acid sequence fragments of SEQ ID NO: 5-34 are included in the amino acid sequences of SEQ ID NO: 2 or 4. Therefore, the amino acid fragments that are associated with SEQ ID NO: 2 are included in the teachings of Stephens et al. Stephens et al teach a total of nine genes named pmp encoding relating proteins. The gene family was located in two clusters with one gene being separate (p. 757, 2nd column, last paragraph and Figure 1A, p. 756). For each of the predicted proteins, the COOH-terminal residue was phenylalanine and some of the family contained predicted cleavable signal peptide leader sequences (PmpC, PmpD, PmpE, and PmpI). These attributes suggest that the proteins are outer membrane proteins. Each was a different size and quite dissimilar in sequence (9 to 42 % amino acid identity), but all were found to be related and shared tetrapeptide repeat motifs organize d in the NH_2-terminal half of the protein (p. 757, 3rd column, 1st paragraph and Figure 1B, p. 756).

Although the reference appears to disclose the same purified polypeptides claimed by the applicant's, the reference does not disclose that the purified polypeptides produced by the same claimed process. However, the purification or production of protein by a particular process does not impart novelty or unobviousness to a protein

when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marsosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Since the Office does not have the facilities for examining and comparing applicant's polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 31-32 and 77-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Probst *(U.S. Patent No. 6,166,177, published December 26, 2000)* in view of Murdin et al *(Infection and Immunity, October 1993, p. 4406-4414)*.

Claims 31-32 and 77-78 are drawn to a vaccine of any one of claims 15 or 20 additionally comprising one or more immunogens selected from the group consisting of

a lipid, lipoprotein, phospholipid, lipooligosaccharide, protein, attenuated organism and inactivated whole cell.

Probst et al teach pharmaceutical compositions and vaccines comprising polypeptides that contain at least one antigenic portion of a Chlamydial antigen (see the Abstract). Probst et al teach that any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions. Probst teach that these carriers include water, saline, alcohol, a fat or wax or a buffer (column 9, lines 14-28). Probst et al teach that a variety of adjuvants may be employed in the vaccines of this invention to enhance the immune response. Probst et al teach that the adjuvants may include aluminum hydroxide, mineral oil, Freund's Incomplete Adjuvant, Freund's Complete Adjuvant, Merck Adjuvant 65, alum, biodegradable microspheres, monophosphoryl lipid A and quil A (column 9, lines 29-41).

Probst et al do not teach the use of additional immunogens.

Murdin et al teach an attenuated poliovirus hybrid expressing a neutralization epitope from the major outer membrane protein of *Chlamydia trachomatis* as well as a 40kDa (high molecular weight) outer membrane protein of *Chlamydia trachomatis* (page 4406, column 2, paragraph 2), in an analogous art for the purpose of inducing a strong mucosal immune response in primates and humans (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the poliovirus-chlamydia hybrid as taught by Murdin et al to the vaccine composition of Probst et al because Probst et al teach that the compositions and vaccines that comprise PMPE together with an additional

Chlamydia antigens, either incorporated into a combination polypeptide or present within a separate polypeptide (column 8, lines 23-27). Therefore, it would have been expected barring evidence to the contrary, that the addition of poliovirus-chlamydia hybrids to the vaccine composition of Probst et al would allow for a powerful subunit vaccine because Murdin et al teach that poliovirus infection induces a strong mucosal immune response in primates and humans which indicate that poliovirus-chlamydia hybrids could become a powerful tool for the development of chlamydial vaccines (see the Abstract).

13. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over ~~in view~~ Stephens et al, *(Science, Volume 282, October 23, 1998)* in view of Schmitt et al (*Molecular Biology Reports Volume 18, 1993, p.223-230).*

Claim 74 is drawn to an isolated recombinant PMPE polypeptide comprising an amino acid sequence of SEQ D NO:2 fused to an amino acid sequence comprising a histidine affinity ($(H)_6$) domain.

Stephens et al teach a protein that is 98% identical to the SEQ ID NO: 2 of the claimed invention. The amino acid sequence fragments of SEQ ID NO: 5-34 are included in the amino acid sequences of SEQ ID NO: 2 or 4. Therefore, the amino acid fragments that are associated with SEQ ID NO: 2 are included in the teachings of Stephens et al. Stephens et al teach a total of nine genes named pmp encoding relating proteins. The gene family was located in two clusters with one gene being separate (p. 757, 2nd column, last paragraph and Figure 1A, p. 756). For each of the

predicted proteins, the COOH-terminal residue was phenylalanine and some of the family contained predicted cleavable signal peptide leader sequences (PmpC, PmpD, PmpE, and PmpI). These attributes suggest that the proteins are outer membrane proteins. Each was a different size and quite dissimilar in sequence (9 to 42 % amino acid identity), but all were found to be related and shared tetrapeptide repeat motifs organize d in the NH_2-terminal half of the protein (p. 757, 3rd column, 1st paragraph and Figure 1B, p. 756).

Stephens et al do not teach the use of a histidine affinity ($(H)_6$) domain (i.e. histidine-tag).

Schmitt et al teach affinity purification of histidine-tagged proteins (see the Title). Schmitt et al teach that the expression of recombinant proteins is a standard technique in molecular biology and a wide variety of prokaryotic as well as eukaryotic expression systems are currently in use. Schmitt et al teach that a limiting step is often that the purification of the expressed recombinant protein that yield low expression levels are employed (see the Abstract). Schmitt et al teach that short amino acid sequences can be fused to the recombinant protein as a tag (page 223). Schmitt et al teach that a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow a high expression of purified protein (page 229).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the histidine-tag as taught by Schmitt et al to the recombinant protein of Stephens et al because Schmitt et al teach that a stretch of 6

histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow purification of the recombinant protein (page 229). It would have been expected barring evidence to the contrary, that the addition of a His-tag to recombinant proteins would allow for high expression of purified protein. The addition of the His-tag is well within the level of skill in the art.

Pertinent Prior Art

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure (Schmitt et al, *Molecular Biology Reports Volume 18, 1993, p.223-230).*

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
April 23, 2002

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600